BACTERIAL PHYSIOLOGY UNIT HARVARD MEDICAL SCHOOL

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Dr. Joshua Lederberg, Rockefeller Univ. York Ave. and 66 St., New York, NY 10021.

Dear Josh,

Thanks for the kind remarks on my July PNAS paper. It was gratifying to have a dividend after I had closed my lab and not expected to make another contribution to the body (as opposed to the sociology) of science. But it was disappointing that the expts. proved indecisive, and I haven't been able to think of better ones, beyond encouraging those with the requisite skills to measure the levels of repair enzymes, etc., in aged cultures. I'm not sure the Hanawalt paper that you sent offers much support for my speculation, since it reports increased repair, rather than increased mutation, as a result of transcription. And thanks for the references on transcription and sensitivity to DNAse.

I also thank you for correcting my distorted recollection of the role of multiple aromatic auxotrophy in the discovery of transduction, and I will send a copy of this letter, as a correction, to Tom Brock. But I think the essence of my earlier interpretation is correct, in the following way. The one-step first mutation in your derivation of LA-22, to a requirement for Tyr plus Phe, could have been a leaky multiple aromatic auxotroph, and the second mutation, adding a requirement for Try, could have been a second, less leaky mutation the same gene — or it could have been located, as you assumed, in a cotransducible trp gene. The map that you sent shows that cotransduction was possible (and I suspect more likely), but I don't know whether these mutations were ever mapped to settle the matter.

I enjoyed your <u>Genetics</u> article on indirect selection. (Have you sent a copy to <u>Cairns?</u>) I particularly appreciated your favorable reference to <u>Landman</u>. His observations on a self-perpetuating phenotypic change have always seemed to me to focus eon an interesting problem, but perhaps its his fault that he didn't build on them. I must also comment on your capacity for far-ranging associations — though I have been deeply interested in Ed Wilson's work on sociobiology (partly because we were both victims of the local ideologists), it never would have occurred to me to link sib selection in bacteria to the problem of the genetic basis of altruism! I have one minor criticism: the term "postadaptation" does not seem to me sufficiently self-explanatory.

I'm enclosing some other items that might interest you. The one on the human genome project is in a new publication, a news bulletin of the NIH Alumni Assoc., which invited it. I wonder whether you share my view that the project has mutated in ways that make it increasingly difficult to justify such a set-aside, when virtually all other areas (except those related to AIDS) are starving. The one to NYRev. Books will probably not be published, and I suspect you would feel that I should not weaken my influence in other areas by coming back to such a touchy subject. But in this case I am not taking up cudgels against affirmative action: rather, it is the extraordinary lengths to which our NAS will now go in order not to rock the boat. letter might profitably have mentioned a consideration that struck me later: just as the Amer. Civil Lib. Assoc. emphasizes the principle that defense of offensive behavior is precisely what tests civil liberties, so it is conflicts between scientific findings and treasured preconceptions that precisely test dedication to the objectivity of science.

Regards,

Bernard D. Davis